

to robotic methods for combinatorial library synthesis and testing, minimizes the storage requirements for combinatorial libraries, and allows for simpler and faster compound identification.

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:2523 CAPLUS

DOCUMENT NUMBER: 137:93369

TITLE: A one-bead, one-stock solution approach to chemical genetics: part 2

AUTHOR(S): Clemons, Paul A.; Koehler, Angela N.; Wagner, Bridget K.; Sprigings, Timothy G.; Spring, David R.; King, Randall W.; Schreiber, Stuart L.; Foley, Michael A.

CORPORATE SOURCE: Howard Hughes Medical Institute at Harvard University, Cambridge, MA, 02138, USA

SOURCE: Chemistry & Biology (2001), 8(12), 1183-1195

CODEN: CBOLE2; ISSN: 1074-5521

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

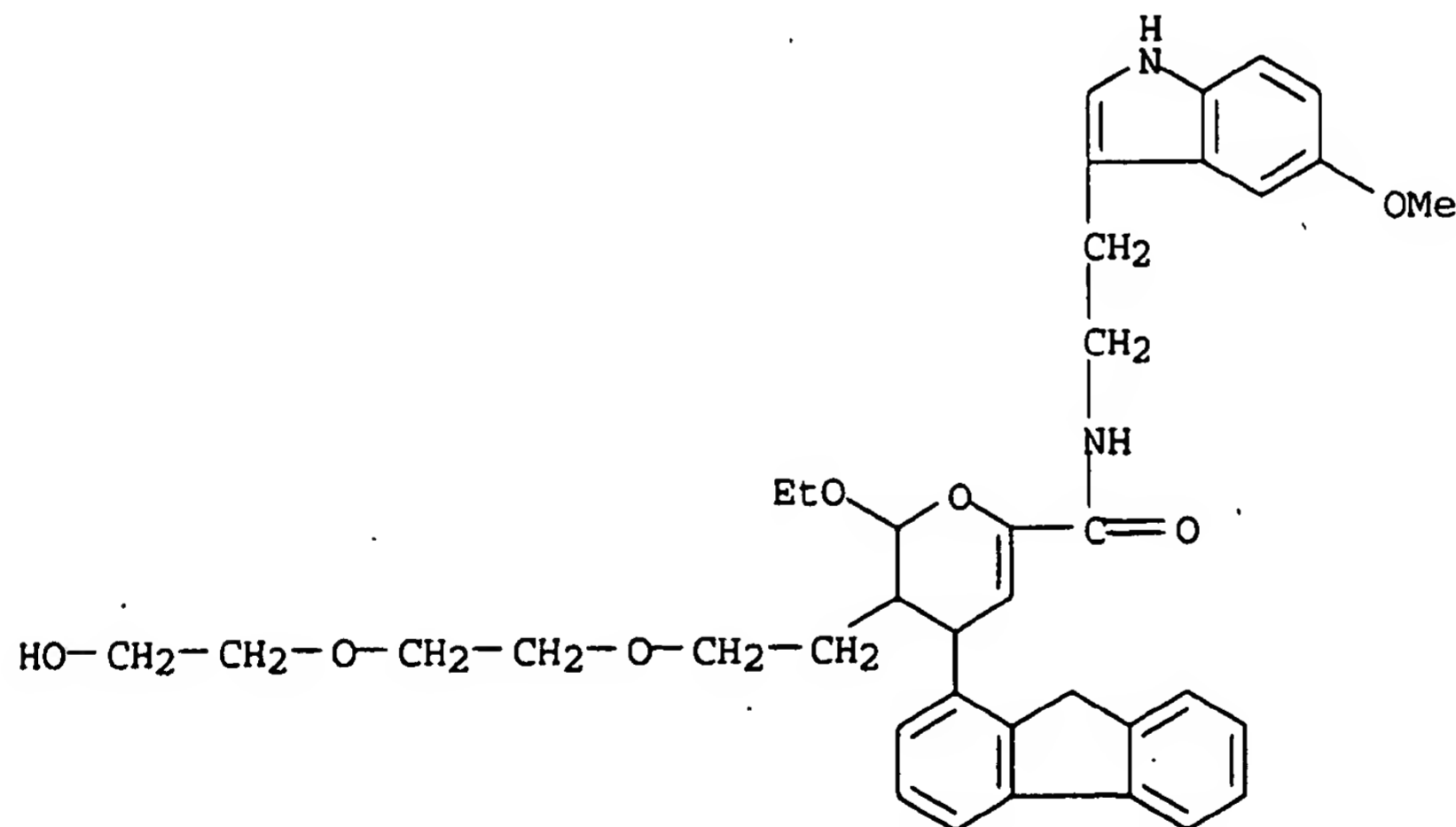
LANGUAGE: English

IT 438625-00-4P 438625-04-8P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation) (bead arraying, processing, and assaying in one-bead, one-stock solution approach to chemical genetics)

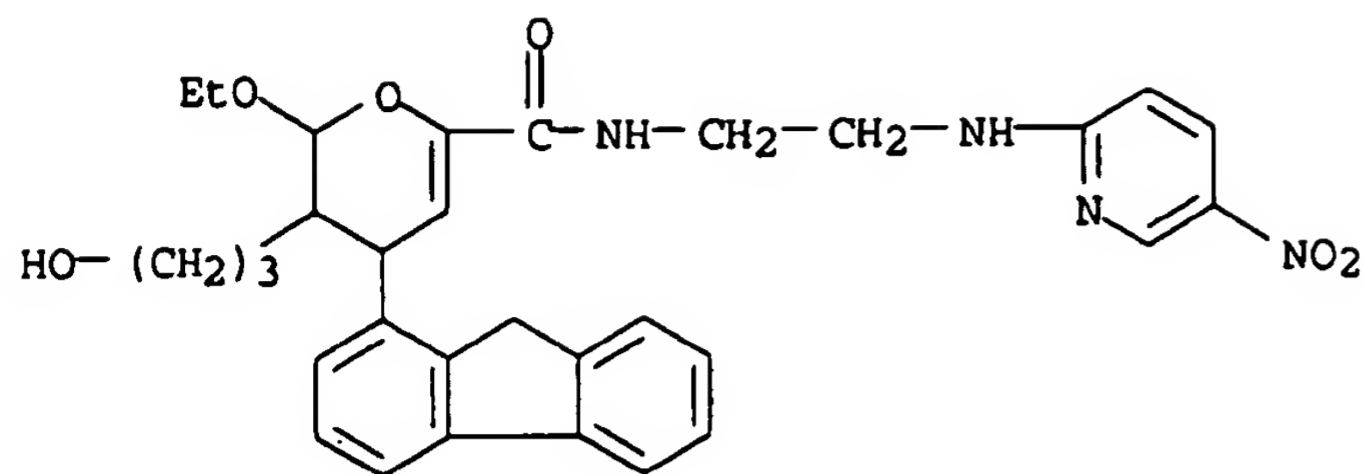
RN 438625-00-4 CAPLUS

CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-1-yl)-3,4-dihydro-3-(2-[2-(2-hydroxyethoxy)ethoxy]ethyl)-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)



RN 438625-04-8 CAPLUS

CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-1-yl)-3,4-dihydro-3-(3-hydroxypropyl)-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]- (9CI) (CA INDEX NAME)



AB Background: Chemical genetics provides a systematic means to study biol. using small mols. to effect spatial and temporal control over protein function. As complementary approaches, phenotypic and proteomic screens of structurally diverse and complex small mols. may yield not only interesting individual probes of biol. function, but also global information about small mol. collections and the interactions of their members with biol. systems. Results: We report a general high-throughput method for converting high-capacity beads into arrayed stock solns. amenable to both phenotypic and proteomic assays. Polystyrene beads from diversity-oriented syntheses were arrayed individually into wells. Bound compds. were cleaved, eluted, and resuspended to generate 'mother plates' of stock solns. The second phase of development of our technol. platform includes optimized cleavage and elution conditions, a novel bead arraying method, and robotic distribution of stock solns. of small mols. into 'daughter plates' for direct use in chemical genetic assays. This library formatting strategy enables what we refer to as annotation screening, in which every member of a library is annotated with biol. assay data. This phase was validated by arraying and screening 708 members of an encoded 4320-member library of structurally diverse and complex dihydropyran carboxamides. Conclusions: Our 'one-bead, multiple-stock solution' library formatting strategy is a central element of a technol. platform aimed at advancing chemical genetics. Annotation screening provides a means for biol. to inform chemical, complementary to the way that chemical can inform biol. in conventional ('investigator-initiated') small mol. screens.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:497822 CAPLUS

DOCUMENT NUMBER: 131:322661

TITLE: Hetero-Diels-Alder reactions of  $\alpha$ -carbonylated styrylphosphonates with enol ethers. High-pressure influence on reactivity and diastereoselectivity

AUTHOR(S): Al-Badri, Hashim; Maddaluno, Jacques; Masson, Serge; Collignon, Noel

CORPORATE SOURCE: Laboratoire d'Heterochimie Organique, INSA de Rouen, UPRES-A 6014 CNRS, 1'IRCOF, Mont-Saint-Aignan, 76131, Fr.

SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1999), (16), 2255-2266

CODEN: JCPRB4; ISSN: 0300-922X

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

10/649,532

prepared A library of 4320 dihydropyrancarboxamides was prepared; claimed title compound (II) was shown to be inhibitory against Eg5 kinesin. Solid support synthesis and decoding methodology is described.

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2002:112577 CAPLUS  
DOCUMENT NUMBER: 136:150765  
TITLE: Decoding products of diversity pathways from stock solutions derived from single polymeric macrobeads  
AUTHOR(S): Blackwell, Helen E.; Perez, Lucy; Schreiber, Stuart L.  
CORPORATE SOURCE: Howard Hughes Medical Institute, Harvard Institute of Chemistry and Cell Biology, Harvard University, Cambridge, MA, 02138, USA  
SOURCE: Angewandte Chemie, International Edition (2001), 40(18), 3421-3425  
CODEN: ACIEF5; ISSN: 1433-7851  
PUBLISHER: Wiley-VCH Verlag GmbH  
DOCUMENT TYPE: Journal  
LANGUAGE: English

IT 394252-96-1P 394253-07-7P 394253-10-2P  
394253-11-3P 394253-12-4P 394253-25-9P  
394253-26-0P 394253-35-1P 394253-42-0P  
394253-49-7P 394253-50-0P 394253-58-8P  
394253-60-2P 394253-61-3P 394253-64-6P  
394253-68-0P 394253-76-0P 395072-36-3P  
395072-37-4P

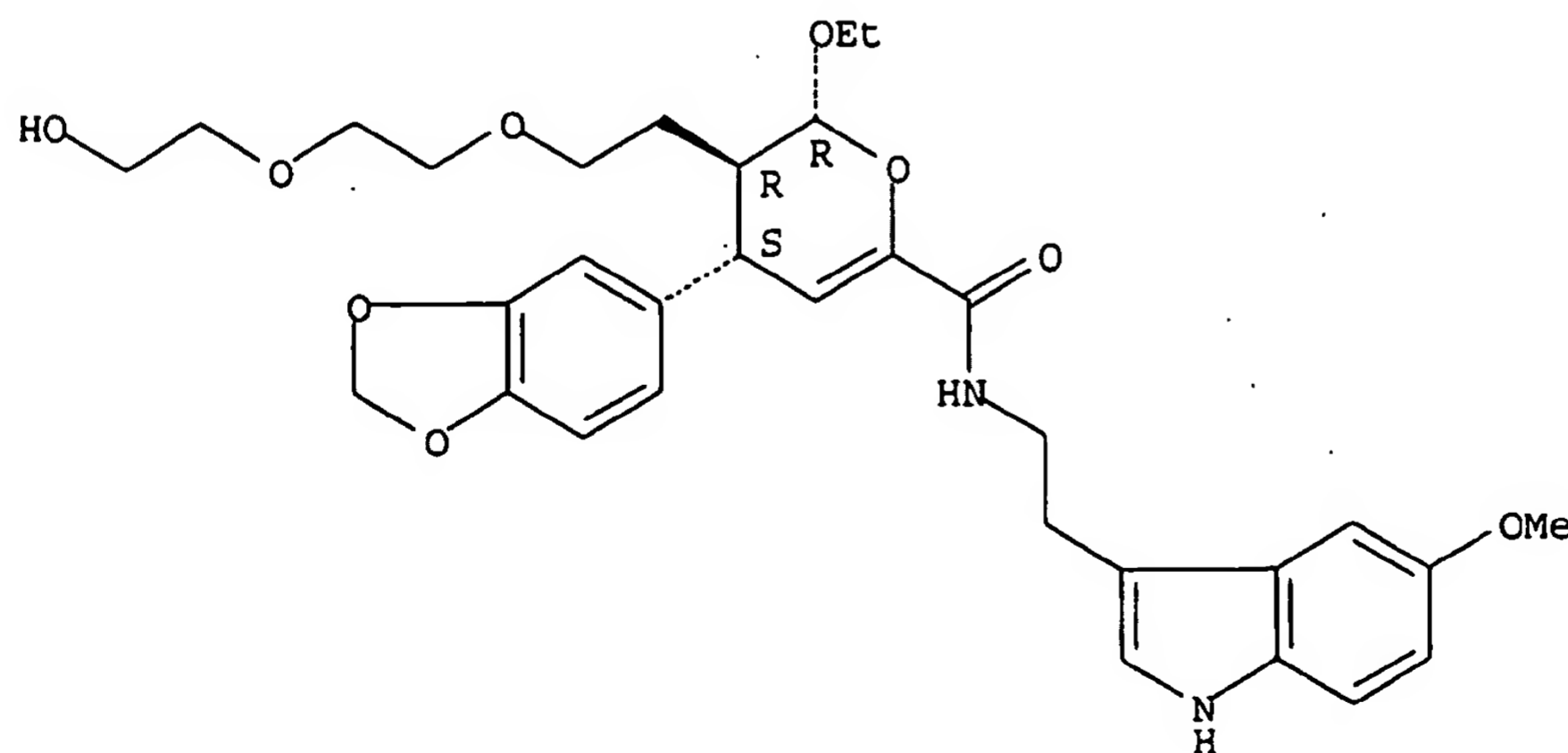
RL: CPN (Combinatorial preparation); CMBI (Combinatorial study); PREP (Preparation)

(chloroarom. diazoketone tags and stock solns. in preparation and decoding and deconvolution of combinatorial libraries on macrobeads and use in preparation of nonracemic dihydropyrancarboxamide combinatorial library)

RN 394252-96-1 CAPLUS

CN 2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-2-ethoxy-3,4-dihydro-3-[2-[2-(2-hydroxyethoxy)ethoxy]ethyl]-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-, (2R,3R,4S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



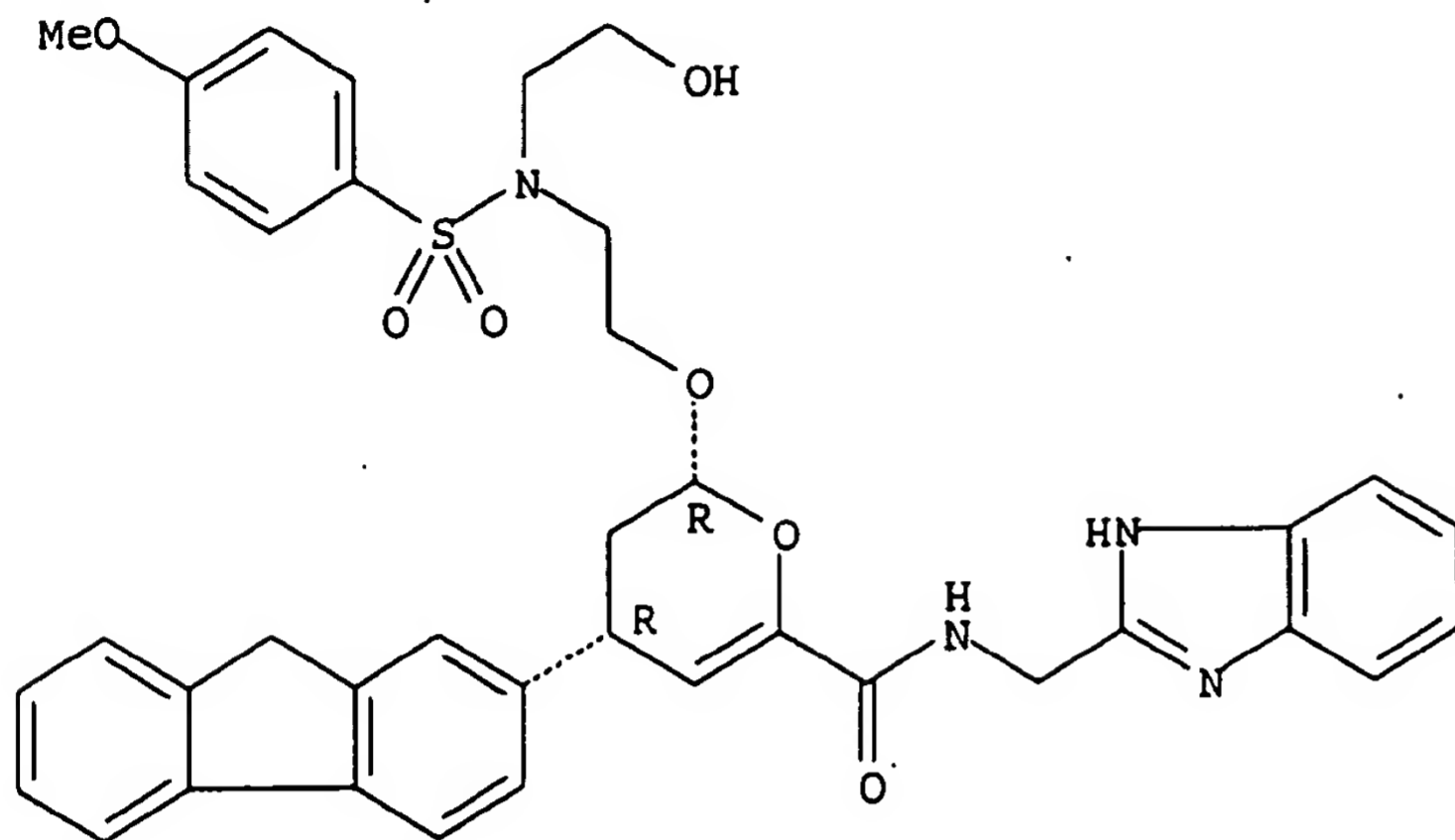
RN 394253-07-7 CAPLUS

CN 2H-Pyran-6-carboxamide, N-(1H-benzimidazol-2-ylmethyl)-4-(9H-fluoren-2-yl)-3,4-dihydro-2-[2-[(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amino]ethoxy]-

10/649,532

, (2R,4R) - (9CI) (CA INDEX NAME)

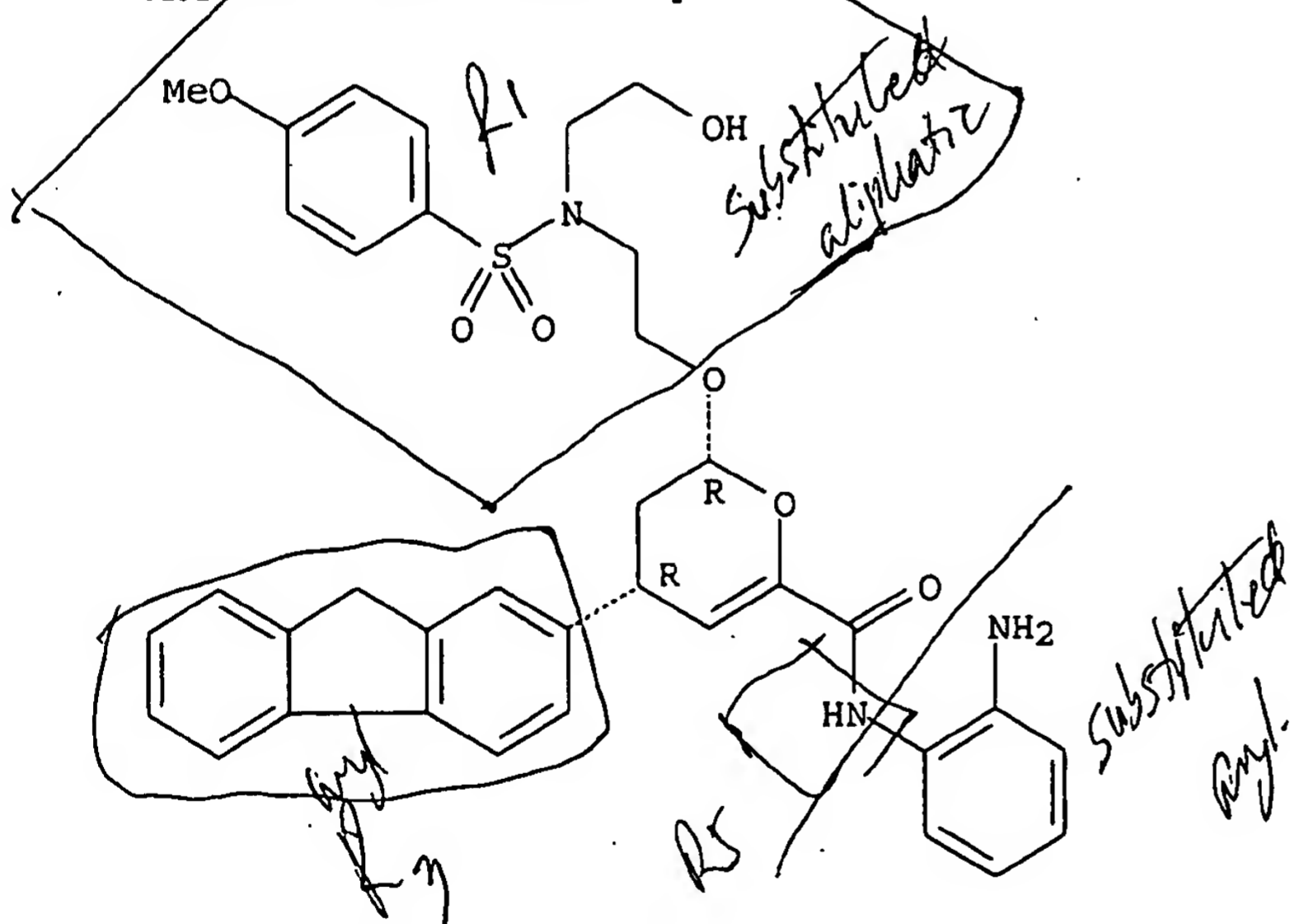
Absolute stereochemistry.



RN 394253-10-2 CAPLUS

CN 2H-Pyran-6-carboxamide, N-(2-aminophenyl)-4-(9H-fluoren-2-yl)-3,4-dihydro-2-[2-[(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amino]ethoxy]-, (2R,4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

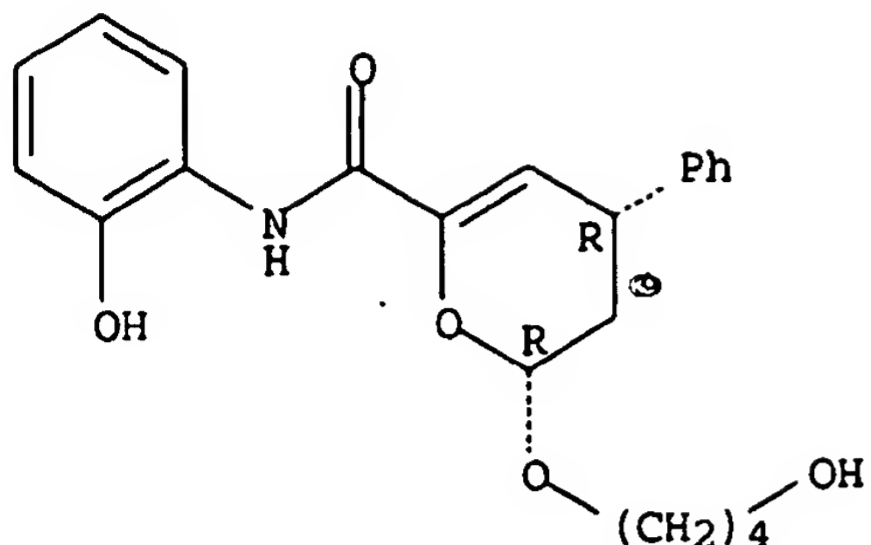


RN 394253-11-3 CAPLUS

CN 2H-Pyran-6-carboxamide, 3,4-dihydro-2-(4-hydroxybutoxy)-N-(2-hydroxyphenyl)-4-phenyl-, (2R,4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

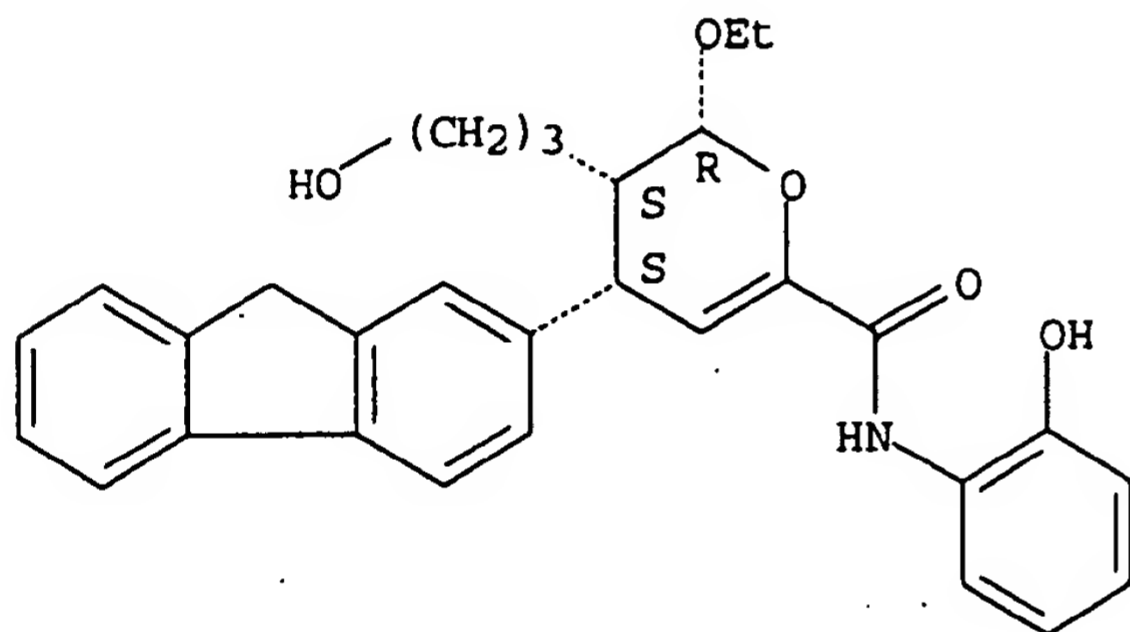
10/649,532.



RN 394253-12-4 CAPLUS

CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-N-(2-hydroxyphenyl)-3-(3-hydroxypropyl)-, (2R,3S,4S)- (9CI) (CA INDEX NAME)

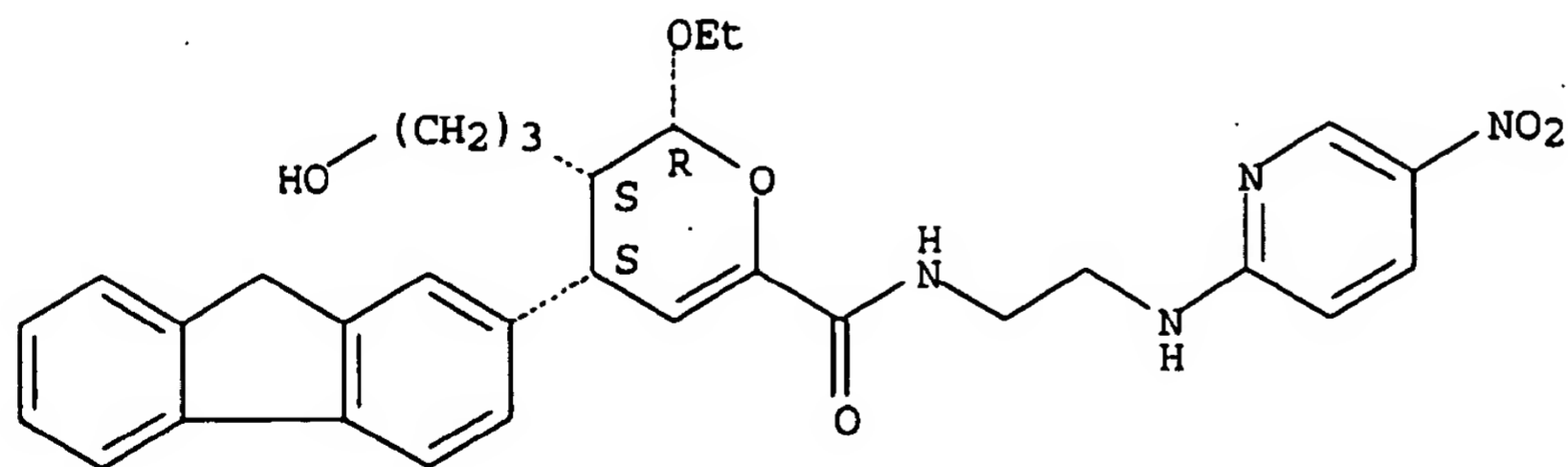
Absolute stereochemistry.



RN 394253-25-9 CAPLUS

CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-3-(3-hydroxypropyl)-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]-, (2R,3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

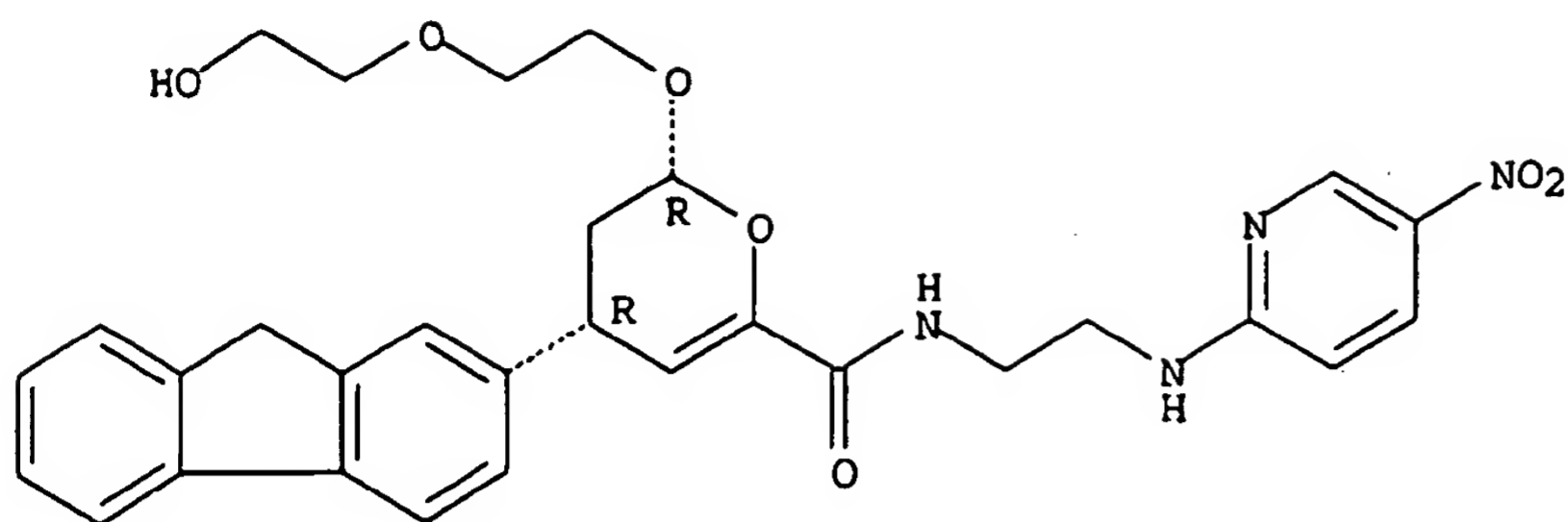


RN 394253-26-0 CAPLUS

CN 2H-Pyran-6-carboxamide, 4-(9H-fluoren-2-yl)-3,4-dihydro-2-[2-(2-hydroxyethoxy)ethoxy]-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

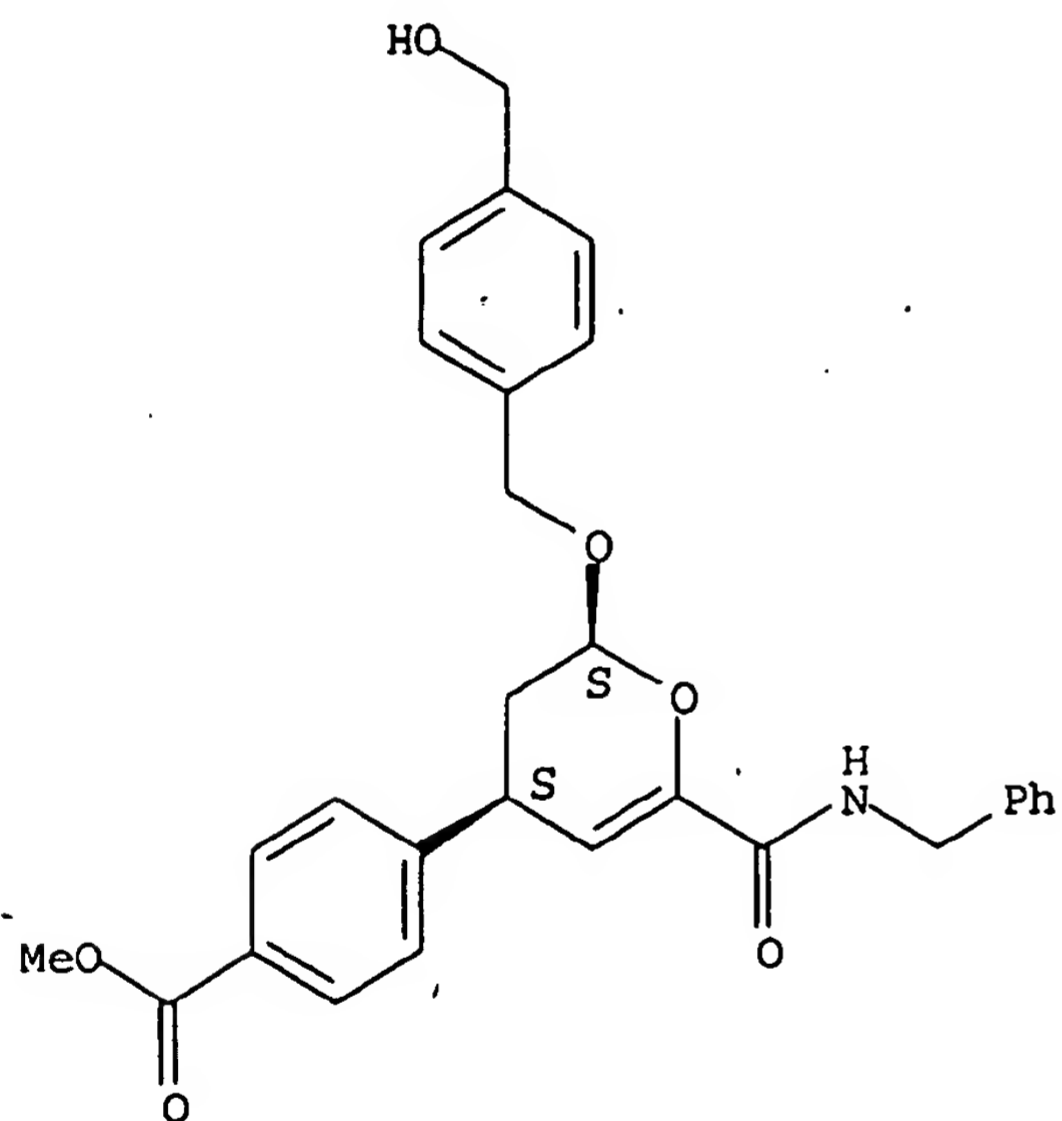
10/649,532



RN 394253-35-1 CAPLUS

CN Benzoic acid, 4-[(2S,4S)-3,4-dihydro-2-[[4-(hydroxymethyl)phenyl]methoxy]-6-[[[(phenylmethyl)amino]carbonyl]-2H-pyran-4-yl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

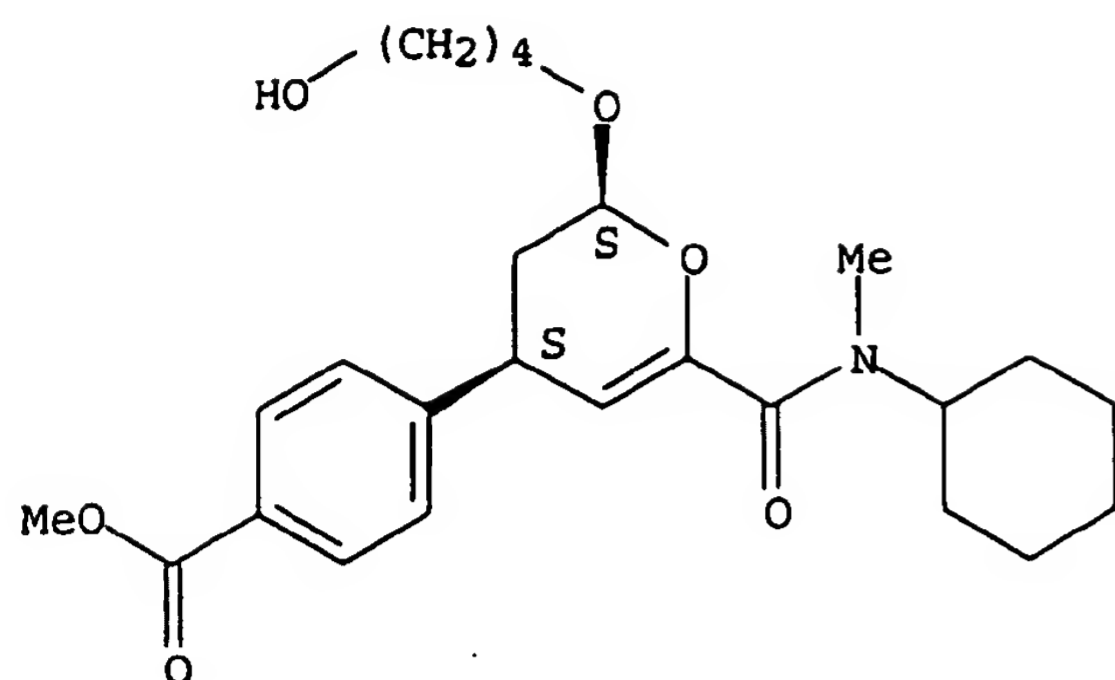


RN 394253-42-0 CAPLUS

CN Benzoic acid, 4-[(2S,4S)-6-[(cyclohexylmethylamino)carbonyl]-3,4-dihydro-2-(4-hydroxybutoxy)-2H-pyran-4-yl]-, methyl ester (9CI) (CA INDEX NAME)

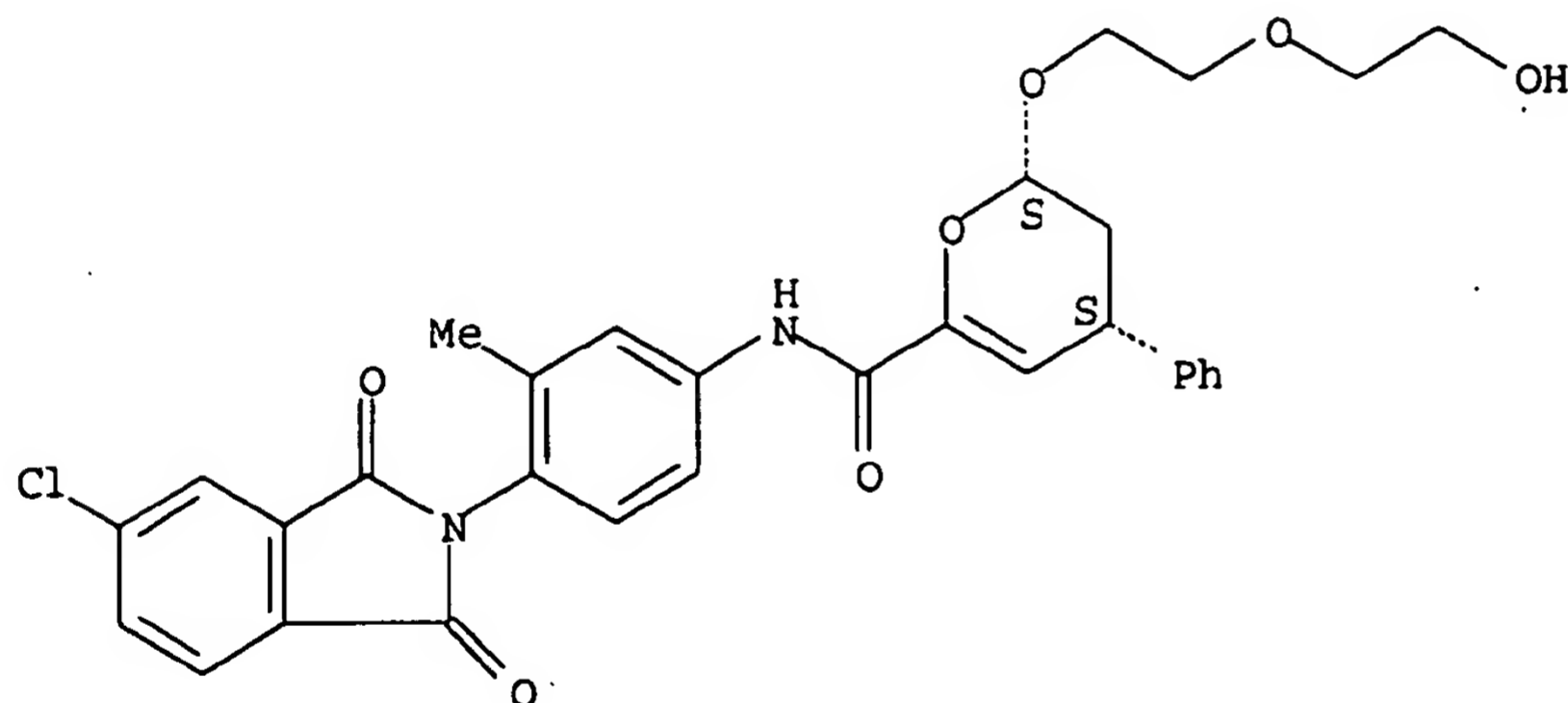
Absolute stereochemistry.

10/649,532



RN 394253-49-7 CAPLUS  
CN 2H-Pyran-6-carboxamide, N-[4-(5-chloro-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-3-methylphenyl]-3,4-dihydro-2-[2-(2-hydroxyethoxy)ethoxy]-4-phenyl-, (2S,4S)-(9CI) (CA INDEX NAME)

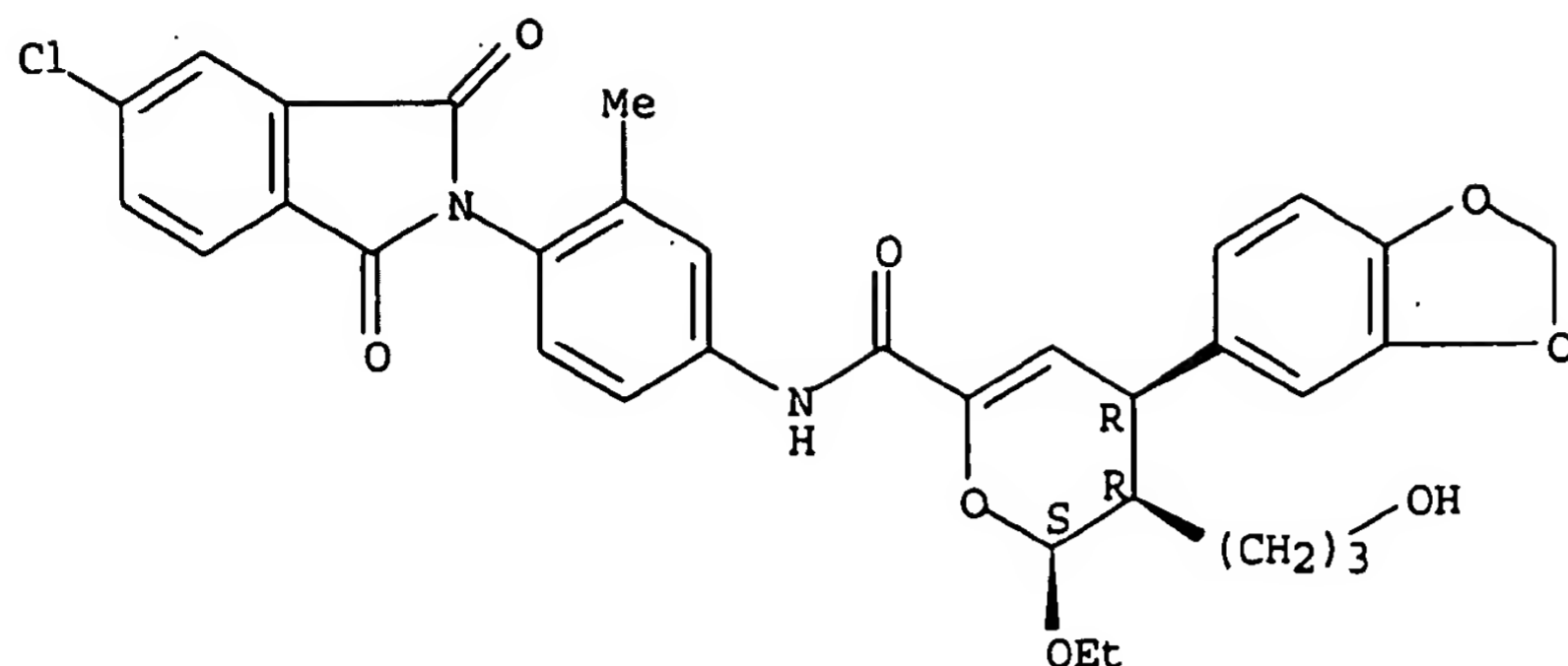
Absolute stereochemistry.



RN 394253-50-0 CAPLUS  
CN 2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-N-[4-(5-chloro-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-3-methylphenyl]-2-ethoxy-3,4-dihydro-3-(3-hydroxypropyl)-, (2S,3R,4R)-(9CI) (CA INDEX NAME)

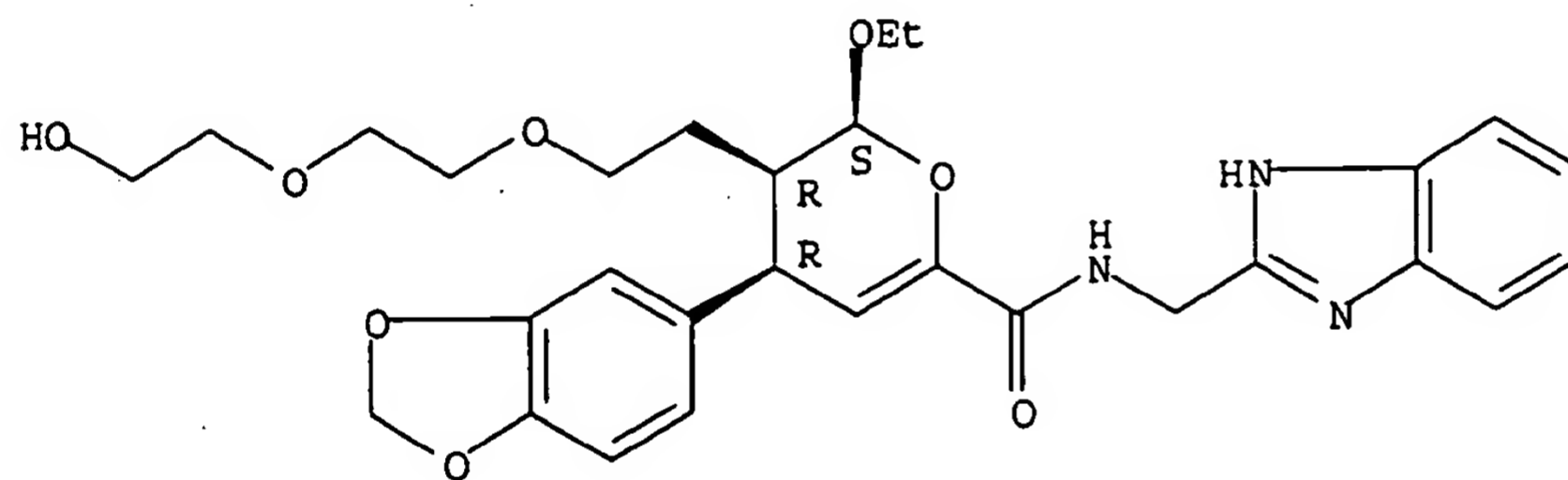
Absolute stereochemistry.

10/649,532



RN 394253-58-8 CAPLUS  
CN 2H-Pyran-6-carboxamide, N-(1H-benzimidazol-2-ylmethyl)-4-(1,3-benzodioxol-5-yl)-2-ethoxy-3,4-dihydro-3-[2-[2-(2-hydroxyethoxy)ethoxy]ethyl]-, (2S,3R,4R)- (9CI) (CA INDEX NAME)

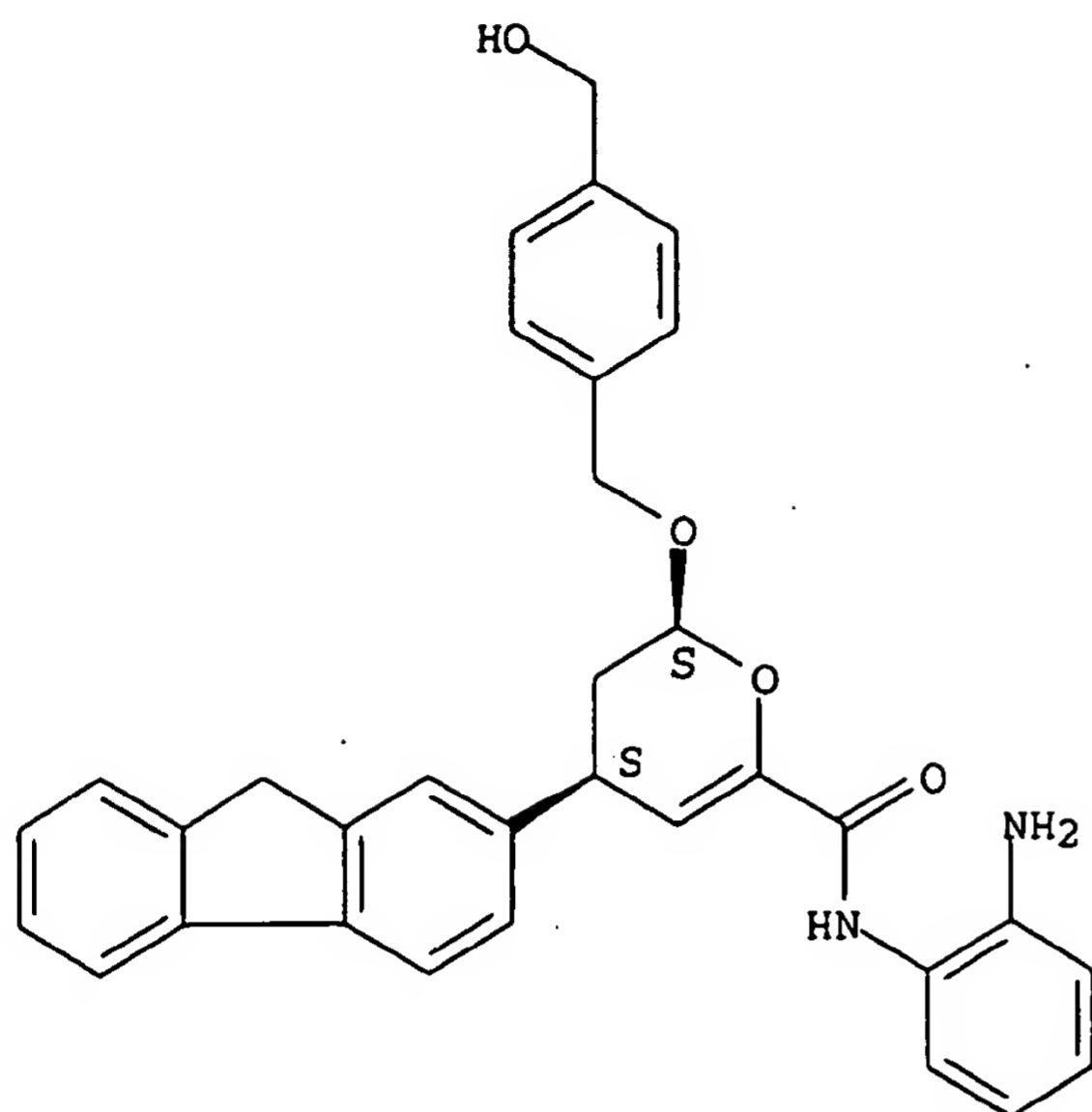
Absolute stereochemistry.



RN 394253-60-2 CAPLUS  
CN 2H-Pyran-6-carboxamide, N-(2-aminophenyl)-4-(9H-fluoren-2-yl)-3,4-dihydro-2-[[4-(hydroxymethyl)phenyl]methoxy]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

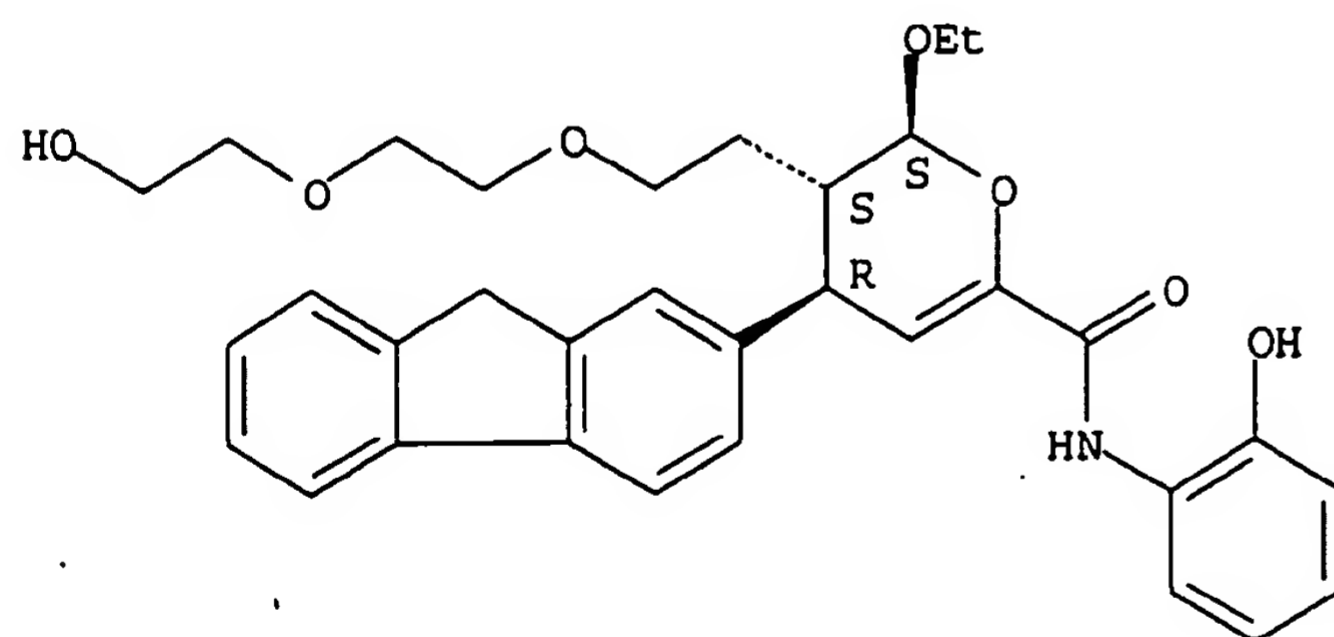
10/649,532



RN 394253-61-3 CAPLUS

CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-3-[2-[2-(2-hydroxyethoxy)ethoxy]ethyl]-N-(2-hydroxyphenyl)-, (2S,3S,4R)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

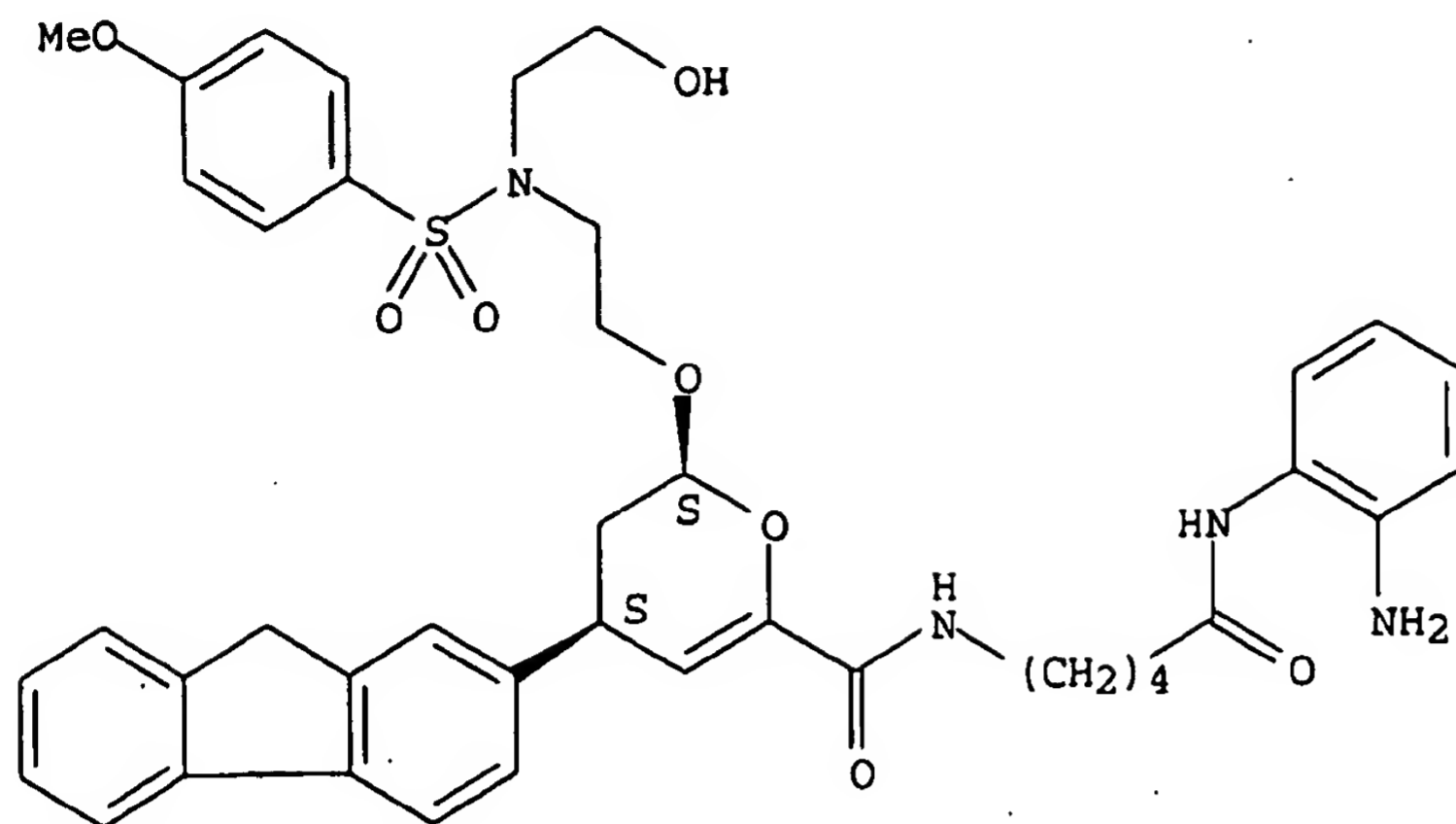


RN 394253-64-6 CAPLUS

CN 2H-Pyran-6-carboxamide, N-[5-[(2-aminophenyl)amino]-5-oxopentyl]-4-(9H-fluoren-2-yl)-3,4-dihydro-2-[2-[(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amino]ethoxy]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

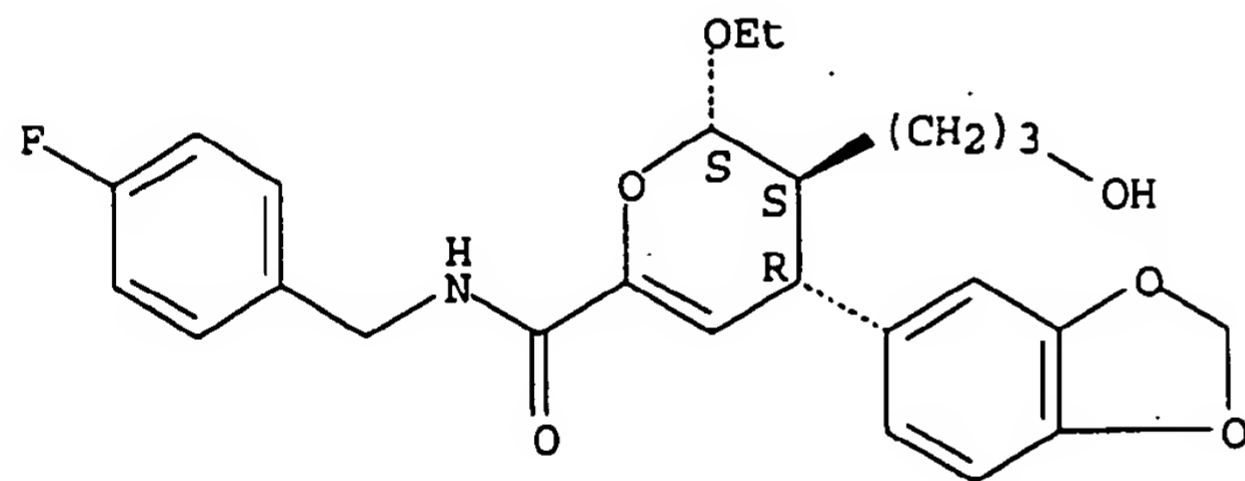
10/649,532



RN 394253-68-0 CAPLUS

CN 2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-2-ethoxy-N-[(4-fluorophenyl)methyl]-3,4-dihydro-3-(3-hydroxypropyl)-, (2S,3S,4R)- (9CI)  
(CA INDEX NAME)

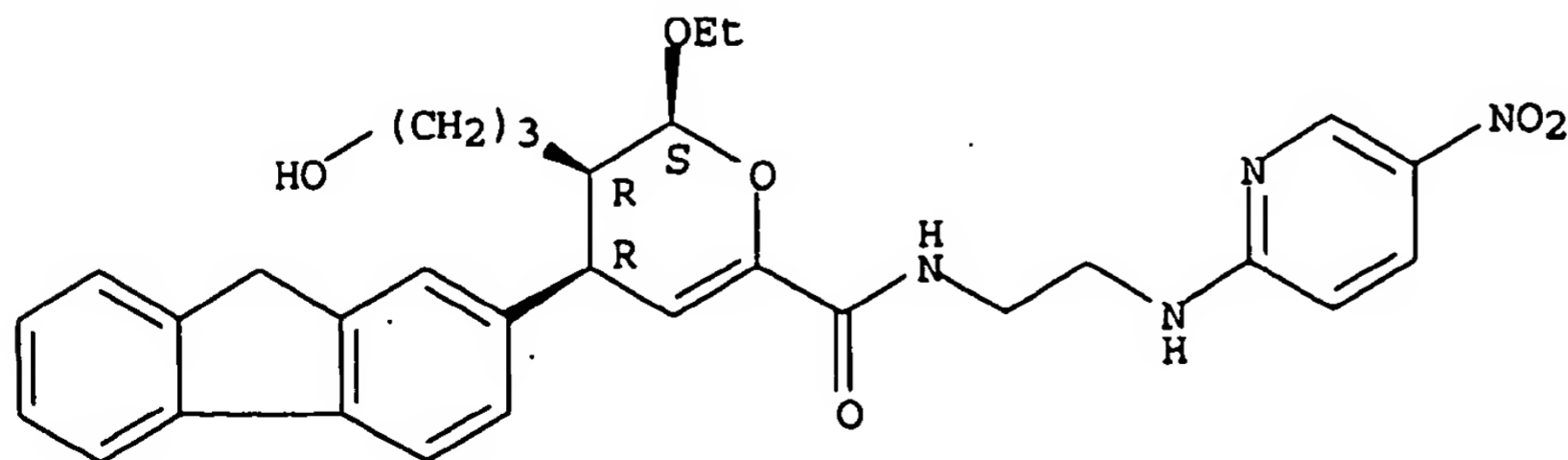
Absolute stereochemistry.



RN 394253-76-0 CAPLUS

CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-3-(3-hydroxypropyl)-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]-, (2S,3R,4R)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



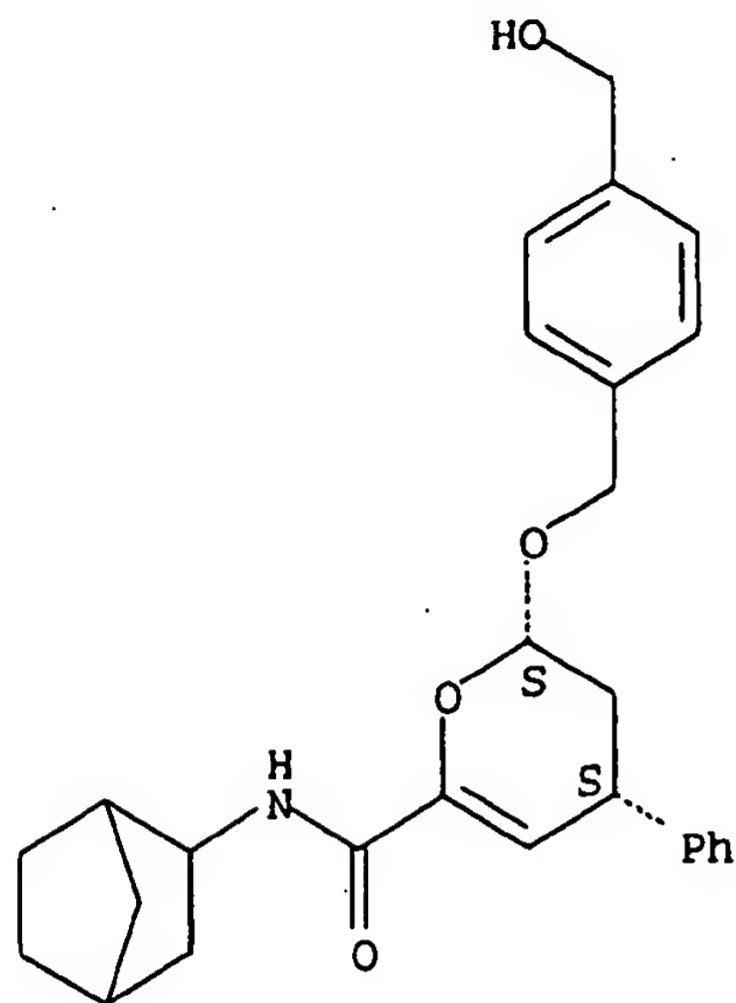
RN 395072-36-3 CAPLUS

CN 2H-Pyran-6-carboxamide, N-bicyclo[2.2.1]hept-2-yl-3,4-dihydro-2-[(4-

10/649,532

(hydroxymethyl)phenyl]methoxy]-4-phenyl-, (2S,4S)- (9CI) (CA INDEX NAME)

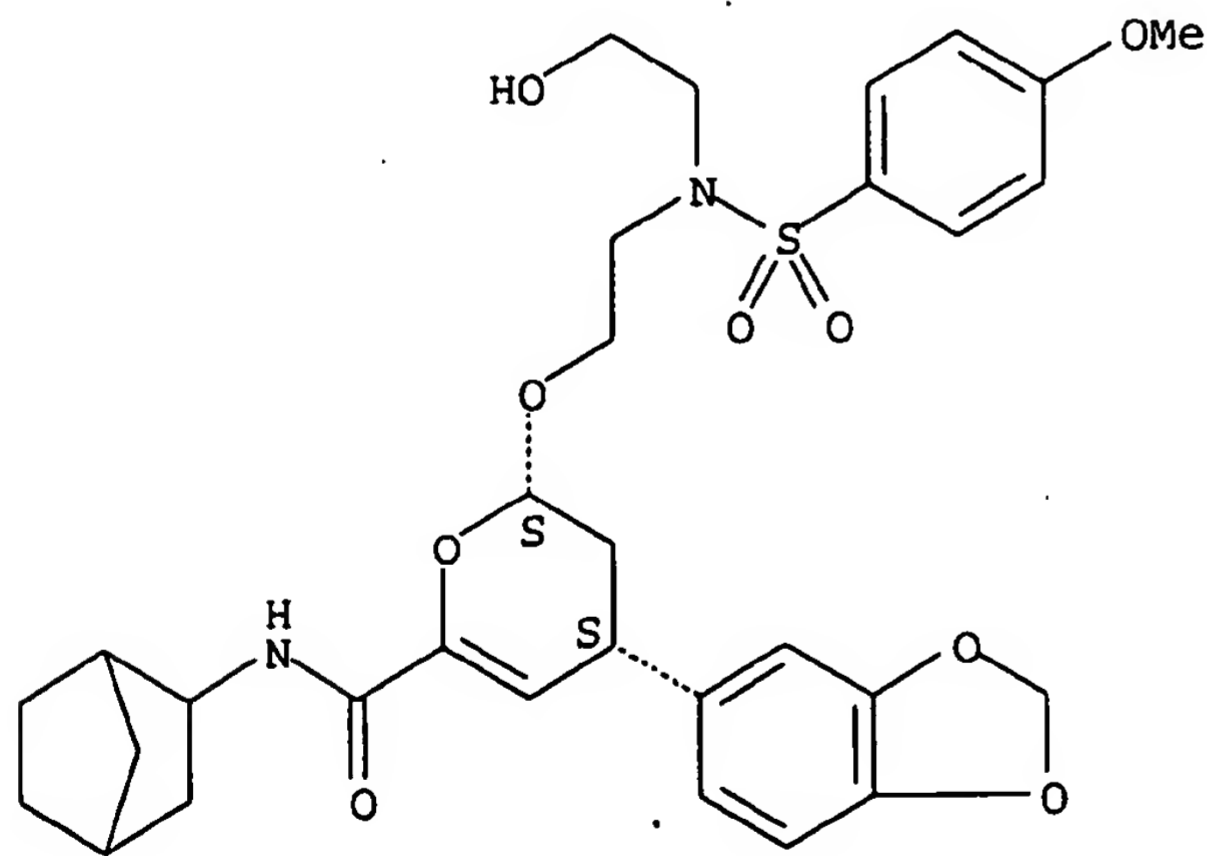
Absolute stereochemistry.



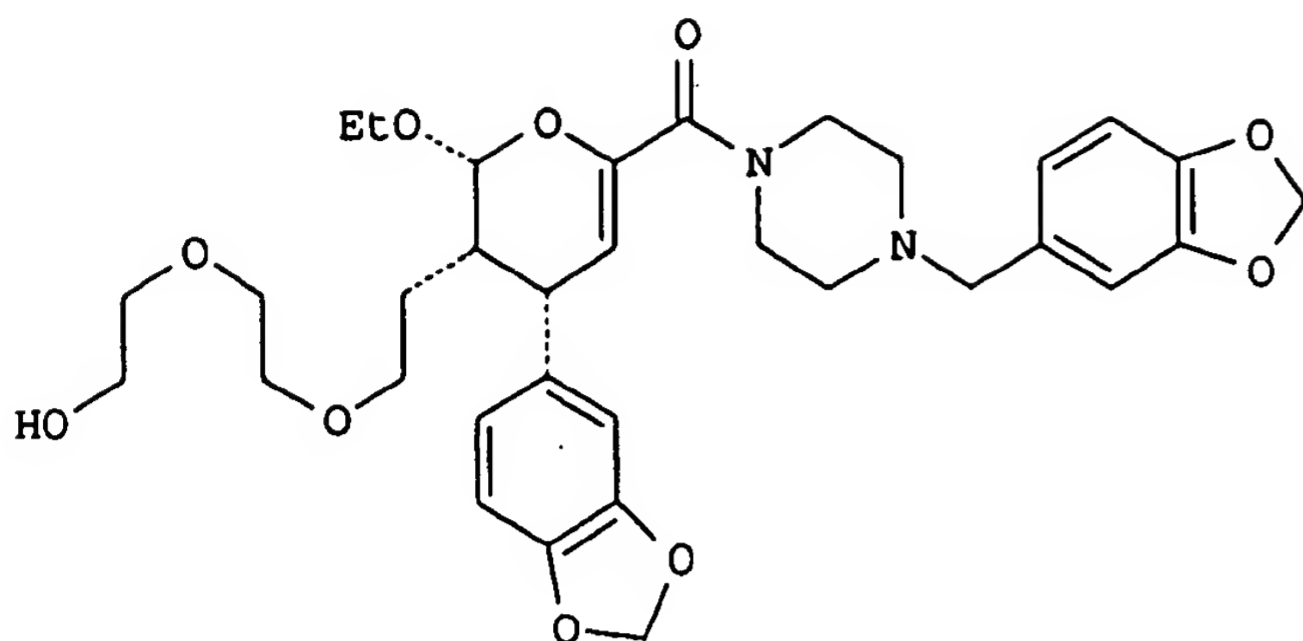
RN 395072-37-4 CAPLUS

CN 2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-N-bicyclo[2.2.1]hept-2-yl-3,4-dihydro-2-[2-[(2-hydroxyethyl) [(4-methoxyphenyl)sulfonyl]amino]ethoxy]-, (2S,4S)- (9CI) (CA INDEX NAME)

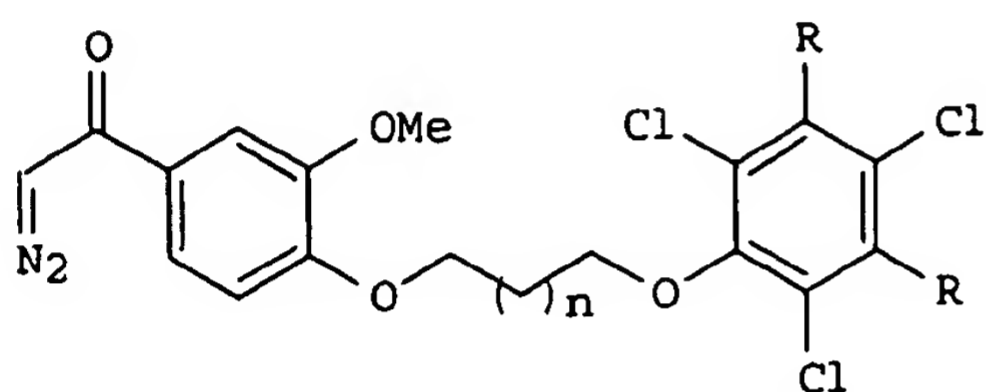
Absolute stereochemistry.



GI



I



II

AB A combinatorial library of nonracemic dihydropyrancarboxamides such as I [prepared on solid phase by the enantioselective Diels-Alder cycloaddn. of resin-bound vinyl ethers with allyl  $\beta,\gamma$ -unsatd.  $\alpha$ -ketoesters in the presence of nonracemic bisoxazoline ligands and copper (II) triflate] using a novel tagging technique for the labeling and identification of members of combinatorial libraries. Chloroarom. diazoketones II ( $n = 1, 7, 14$ ;  $R = H, Cl$ ) were used as tagging agents to identify the sequence of reactions to which a resin bead had been subjected; treatment of a resin bead with II in the presence of dirhodium tetrakis(triphenylacetate) yielded a polystyrene resin containing a fraction of chloroaralkyl cycloheptatriene moieties (formed by ring expansion of the polystyrene Ph groups). Oxidative cleavage of the tags with ceric ammonium nitrate liberated the chloroarom. portion of the tags; treatment of the tags with N,O-bis(trimethylsilyl)acetamide and gas chromatog. yielded masses corresponding to the sequence of reactions to which beads were subjected and thus their identities. The tags could be decoded either directly from a bead before compound cleavage, from a bead after compound cleavage, or from compound stock solns. (generated by compound cleavage and dissoln. of a fraction of the liberated compds. in THF/H<sub>2</sub>O). Decoding compound stock solns. was the most effective method of identifying library members; compds. were identified by tag cleavage of solns. containing 1 or 5% of the compound cleaved from a single bead. Stock solns. were decoded most effectively because a fraction of the library member on a given bead was tagged with the chloroarom. diazoketone in addition to the polystyrene resin (due to the high-loading resin used) and because oxidative cleavage of the tags with CAN proceeded more readily in solution than on solid support. A sublibrary of 108 beads chosen from the larger combinatorial library was decoded by this procedure; of the 108 compds., 107 were successfully decoded. Four different synthetic pathways were found to be compatible with the diazoketone tagging methodol. (no data). The use of stock solns. for the decoding and deconvolution of combinatorial libraries is amenable